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DEPARTMENT OF HEALTH & HUMAN SERVICES

New York District

Food & Drug Administration
300 Pearl Street, Suite 100
Buffalo, NY 14202

July 22, 2004

WARNING LETTER NYK 2004-25

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Dennis P. Borrello, President
Ultra-Seal Corporation
521 Main Street
New Paltz, New York 12561-1609

Dear Mr. Borrello:

An inspection of your drug repacking and labeling facilities located in New Paltz, New York, conducted by Investigator Demitria J. Argiropoulos between March 2-8, 2004, found significant deviations from current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, Parts 210 and 211). Such deviations cause your finished pharmaceuticals to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

In addition, during our inspection of your firm Investigator Argiropoulos documented that a complete failure of quality control as described in the deficiencies below resulted in distribution of a misbranded drug product, "BDI Mini Ephedrine" tablets. The BDI Mini Ephedrine tablets are misbranded under section 502(a) of the Federal Food, Drug, and Cosmetic Act because the label fails to bear an accurate declaration of the quantity of ephedrine HCl present in each tablet. The drug contained the active ingredients 25 mg Ephedrine HCl and 200 mg Guaifenesin, but was labeled as containing 12.5 mg Ephedrine HCl and 200 mg Guaifenesin. The recall action undertaken by your firm was evaluated as Class I because this error could cause serious adverse consequences and/or death.

Our inspection revealed the following deviations:

1. Strict control is not exercised over labeling issued for use in drug product labeling operations; 21 CFR 211.125(a).

   For example, the firm lacks detailed written procedures in place to ensure that any additional rolls of labeling brought to packaging lines from warehouse stock during multiple days of operation are adequately examined for identity and conformity to batch record specifications before being issued for use for the same batch. This failure led to the recall of 308,832 six-count packets of mislabeled drug product tablets. In addition, the firm lacks procedures to establish control over labels which are similar in size, shape, and color for different products in order to prevent mix-ups.

2. Labeling materials issued for a batch are not carefully examined for identity and conformity to labeling specified in the master or batch production records; 21 CFR 211.125(b).

For example, production records for Lot #3L001 document that a total of 150 samples taken during 10 different times in the manufacturing process passed the "Correct Fill and Correct Specimen" examination, even though all of the samples were mislabeled. In addition, after inaccurate batch record examination, the final product, although mislabeled, was approved for conformity to batch record specifications by the firm's quality control department.

3. Drug product production and control records are not reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed; 21 CFR 211.192.

   For example, quality control department did not review, approve, and release product prior to shipment. For example, Lot #3L001 of BDI Mini Ephedrine 25mg Ephedrine HCl/ 200mg Guafenesin was shipped into interstate commerce on December 19, 2003 prior to the quality control department reviewing and approving the lot for release on December 23, 2003. In addition, the firm failed to follow their procedure (SOP #309, Master Batch Record Generation and Initiation of Production Batch Control Records) which requires that the quality control department release products prior to shipment.

4. Employees engaged in the processing and packing of a drug product lack the training required to perform their assigned functions; 21 CFR 211.25(a).

   For example, the incorrect labeling was selected, picked, and issued to the packaging line on December 11-12, 15, and 16, 2003. This failure led to the repacking and distribution of mislabeled drug products. Employees did not receive adequate training to prevent this from occurring. Review of employees training records from 2001 - 2003 revealed that there was no documentation of training for the warehouse employees responsible for selecting and issuing labels to the packaging lines.

5. The written record or copy of the record of an investigation of a complaint conducted in relation to the failure of a batch or any of its components to meet any of its specifications is not maintained at the establishment where the investigation occurred; 21 CFR 211.198(b)(2).

   For example, the firm failed to document the receipt, investigation, and corrective action taken by the firm regarding customer complaint received on February 9, 2004 for labeling errors on BDI Mini Ephedrine, Lot #3L001, expiration date, November 2005. In addition, the firm failed to follow their procedure (SOP #409A, Procedure for Handling Written and Oral Complaints), which requires investigation of complaints.

The above is not intended to be an all-inclusive list of violations. As a manufacturer of finished pharmaceuticals, you are responsible for assuring that your overall operation and the products you repack, re-label, and distribute are in compliance with the Act. Please be aware that you should make systematic CGMP corrections to this facility and any others under your control.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so they may take this information into account when considering the award of contracts.

You should take prompt action to correct these violations and to establish procedures to prevent recurrence. Failure to promptly correct these violations may result in regulatory action without further notice, such as seizure and/or injunction.

We acknowledge receipt of your written response dated March 8, 2004, which addresses the inspectional observations on the Form FDA 483 issued at the close of the inspection. Corrective actions addressed in your letter may be referenced in your response to this letter, as appropriate. However, your response to items 1-5 did not provide sufficient detail to fully assess the adequacy of the corrective actions. Our evaluation of your response follows, and is numbered to correspond to the items listed on the Form FDA 483:

1. Your response fails to identify the procedures which were amended or provide a detailed explanation of the changes.

2. Your response fails to identify the procedures which were modified and provide an explanation of the changes.

3. Your response fails to provide an explanation of how replacing the Quality Control manager will bring about compliance. Please ensure that the new Quality Control manager has the education, training, and experience, or any combination thereof, to perform assigned functions to provide assurance that the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to posses. In addition, you referred to a procedure which was not identified.

4. You indicated new procedures would be written. Please identify each of these procedures and include the scope and purpose. In addition, your response fails to address a potential problem which involves a possible language barrier involving warehouse employees who have the task of selecting labels written in English. You indicated to our investigator that the warehouse employees could speak, but not read, English.

5. Your response only indicated that certain in-house reports associated with a labeling complaint and a Class I recall had been completed. Please provide an explanation of why a thorough investigation was not initiated prior to our inspection as required by regulations and your procedures. In addition, your response fails to indicate what steps you took upon learning that a mislabeled lot was shipped prior to release by the quality control department. For example, you did not suggest performing a records search comparing release dates by the quality control department and shipping dates, followed by remedial follow up where indicated.

You should notify this office in writing, within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, please state the reason for the delay and the time by which the corrections will be completed. Correspondence should be directed to Compliance Officer William J. Thompson, U.S. Food and Drug Administration, at the above address, by telephone, 716-551-4461 (3124).

Sincerely yours,

Jerome G. Woyshner
District Director